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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/828,644	04/06/2001	Gabriel Vogeli	00196US1/PHRM-0330	5533

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EXAMINER
ULM, JOHN D

ART UNIT	PAPER NUMBER
1646	12

DATE MAILED: 04/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/828,644	Vogeli
Examiner	**Art Unit**
John Ulm	1646

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) X Responsive to communication(s) filed on *Jan 6, 2003* .

2a) ☐ This action is **FINAL**. 2b) X This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) X Claim(s) *1-31 and 33-124* is/are pending in the application.

4a) Of the above, claim(s) *1-29, 36-89, and 93-124* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) X Claim(s) *30, 31, 33-35, and 90-92* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) X Information Disclosure Statement(s) (PTO-1449) Paper No(s). *4, 7-9*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____

1) Claims 1 to 31 and 33 to 124 are pending in the instant application. Claim 92 has been amended and claim 32 has been canceled as requested by Applicant in Paper Number 11, filed 06 January of 2003.

2) Claims 1 to 29, 36 to 89, 93 to 124, and claims 30, 31 and 33 to 35 in so far as they relate to an amino acid sequence recited therein other than SEQ ID NO:67, are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 11. The traversal is on the ground(s) that a search of the different inventions in a single application would pose no undue burden. This is not found persuasive because M.P.E.P. 803 states that:

> " For purposes of the initial requirement, a serious burden on the examiner may be prima facie shown if the examiner shows by appropriate explanation either separate classification, separate status in the art, or a different field of search as defined in MPEP § 808.02. That prima facie showing may be rebutted by appropriate showings or evidence by the applicant."

Serious burden was shown in the original requirement by the separate classification and separate status in the art of the different inventions. Applicant has provided neither a showing or evidence to the contrary.

The requirement is still deemed proper and is therefore made FINAL.

Applicant has further traversed this restriction on the premise that the Markush Group recited in the claims should have been treated as an election of species. M.P.E.P. 2173.05(h)

states that "when the Markush group occurs in a claim reciting a process or a combination **(not a single compound)**, it is sufficient if the members of the group are disclosed in the specification to possess at least one property in common which is mainly responsible for their function **in the claimed relationship**, and it is clear from their very nature or from the prior art that all of them possess this property". It further states that "[w]here a Markush expression is applied only to a portion of a chemical compound, **the propriety of the grouping is determined by a consideration of the compound as a whole**, and does not depend on there being a community of properties in the members of the Markush expression" (emphasis added). The instant claims recite an improper Markush group because they refer to fifty eight different amino acid sequences which do not reflect a single inventive concept.

3) Claims 30, 31 and 33 to 35 stand objected to as reciting an improper Markush Group for those reasons of record as applied to claims 1 to 39, 41, 49, 53 to 59, 66 to 73 and 78 to 81 in section 2 of Paper Number 6 and as explained above. Correction is required.

4) Claims 30, 31, 33 to 35 and 90 to 92 stand objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim for those reasons of record in section 3 of Paper Number 6. Applicant **is required** to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. See MPEP § 608.01(n):

> ""Infringement Test" for dependent claims. The test for a proper dependent claim is whether the dependent claim includes every limitation of the parent claim. The test is not

whether the claims differ in scope. A proper dependent claim shall not conceivably be infringed by anything which would not also infringe the basic claim."

Each of these claims can be infringed by an isolated polypeptide that does not infringe the isolated nucleic acid molecule of the independent claims from which these claims ultimately depend. Further, claim 92 can be infringed by an isolated polypeptide which does not infringe claim 90 or 91, from which claim 92 depends. Correction is required.

5) Claim 91 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 90. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

6) Tables 1 to 5 of the instant specification do not comply with 37 C.F.R. 1.52 (b) with respect to spacing and/or font size. 37 C.F.R. 1.52 (b) states that:

" Except for drawings, the application papers (specification, including claims, abstract, oath or declaration, and papers as provided for in this part) and also papers subsequently filed, must have each page plainly written on only one side of a sheet of paper, with the claim or claims commencing on a separate sheet and the abstract commencing on a separate sheet. See §§ 1.72(b) and 1.75(h). The sheets of paper must be the same size and either 21.0 cm. by 29.7 cm. (DIN size A4) or 21.6 cm. by 27.9 cm. (8 ½ by 11 inches). Each sheet must include a top margin of at least 2.0 cm. (3/4 inch), a left side margin of at least 2.5 cm. (1 inch), a right side margin of at least 2.0 cm. (3/4 inch), and a bottom margin of at least 2.0 cm. (3/4 inch), and no holes should be made in the sheets as submitted. The lines of the specification, and any amendments to the specification, must be 1 ½ or double spaced. The pages of the specification including claims and abstract must be numbered consecutively, starting with 1, the numbers being centrally located above or preferably, below, the text. See § 1.84 for drawings.

37 C.F.R. 1.58 © states that:

Chemical and mathematical formulae and tables must be presented in compliance with § 1.52(a) and (b), except that chemical and mathematical formulae or tables may be placed in a landscape orientation if they cannot be presented satisfactorily in a portrait orientation. Typewritten characters used in such formulae and tables must be chosen from a block (nonscript) type font or lettering style having capital letters which are at least 0.21 cm. (0.08 inch) high (e.g., elite type). A space at least 0.64 cm. (1/4 inch) high should be provided between complex formulae and tables and the text. Tables should have the lines and columns of data closely spaced to conserve space, consistent with a high degree of
legibility.

Correction is required.

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

7) Claims 30, 31, 33 to 35 and 90 to 92 are rejected under 35 U.S.C. § 101 because they are drawn to an invention with no apparent or disclosed specific and substantial credible utility. The instant application has provided a description of an isolated DNA encoding a putative G protein-coupled receptor protein and the protein encoded thereby. The instant application does not disclose a specific biological role for this protein or its significance to a particular disease, disorder of physiological process which one would wish to manipulate for a desired clinical effect.

It is clear from the instant specification that the receptor protein described therein is what is termed an "orphan receptor" in the art. This is a protein whose cDNA has been isolated because of its similarity to known proteins. There is little doubt that, after complete characterization, this protein may be found to have a specific and substantial credible utility. This

further characterization, however, is part of the act of invention and until it has been undertaken Applicant's claimed invention is incomplete. Whereas one could readily employ a putative receptor protein of the instant invention in an assay to identify ligands thereto the information obtained thereby would be of little use until one discovers the identity of those physiological processes moderated by that putative receptor. Because the instant specification has failed to credibly identify a physiological process which has been shown to be influenced by the activation or inhibition of a putative receptor protein of the instant invention an artisan would have no way of predicting what effects the administration of that ligand to an organism would have. If one can not predict the effects that the administration of a ligand of the putative receptor of the instant invention is going to have on an organism then it is unclear as to what practical benefit is derived by the public from the identification of that ligand.

The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. § 101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility. The court held that:

"The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", " [u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", " [i]t is not a reward for the search, but compensation for its successful conclusion."

The instant claims are drawn to a protein of as yet undetermined function or biological significance. There is insufficient evidence of record or credible line of reasoning that would support the conclusion that a protein of the instant invention is associated with any one or more of the plurality of causally unrelated diseases and disorders listed on pages 33, 41 and 48 to 51 of the instant specification. Until some actual and specific significance can be attributed to the protein identified in the specification as "nGPR-x" , or the gene encoding it, the instant invention is incomplete. The protein of the instant invention is a compound known to be structurally analogous to proteins which are known in the art as G protein-coupled receptors. In the absence of a knowledge of the natural ligands or biological significance of this protein, there is no immediately obvious patentable (practical) use for it. To employ a protein of the instant invention in the identification of substances which inhibit or induce its activity is clearly to use it as the object of further research which has been determined by the courts to be a utility which, alone, does not support patentability. Since the instant specification does not disclose a specific "real world" use for "nGPR-x" in its currently available form then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. § 101 as being useful.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8) Claims 30, 31, 33 to 35 and 90 to 92 are rejected under 35 U.S.C. § 112, first paragraph, as failing to adequately teach how to use the instant invention for those reasons given above with regard to the rejection of these claims under 35 U.S.C. § 101.

9) Claims 30, 31, 33 to 35 and 90 to 92 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims encompass an isolated polypeptide comprising an amino acid sequence "homologous" to the amino acid sequence presented in SEQ ID NO:67 of the instant application. The instant specification, however, only contains an adequate written description of a single protein within the recited genus and this protein comprises the amino acid sequence presented in SEQ ID NO:67. No homologous protein is described in the instant specification. Whereas the instant claims encompass a potentially large genus of isolated polypeptides comprising different amino acid sequences, the instant specification does not provide a detailed description of a sufficient number of species of nucleic acids with the claimed genus to establish possession of that genus. The description of a single isolated nucleic acid encoding a single protein does not serve as an adequate basis for the relatively large genus of nucleic acids encompassed by the instant claims.

Further, claims 34 and 35 expressly require an "allelic variant" of a polypeptide comprising the amino acid sequence presented in SEQ ID NO:67 of the instant application. The instant specification, however, does not contain an adequate written description of an "allelic variant" of a polypeptide comprising the amino acid sequence of SEQ ID NO:67. In the decision of *The Regents of the University of California v. Eli Lilly and Company*, 43 USPQ2d 1398 (CAFC 1997), the court held that:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc. , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood , 107 F.3d at 1572, 41 USPQ2d at 1966.

The instant specification does not provide a precise description of an isolated protein which is homologous to or an allelic variant of SEQ ID NO:67 "by structure, formula, chemical name, or physical properties".

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10) Claims 30, 31, 33 to 35 and 90 to 92 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

10.1) Claims 30, 31, 33 to 35 and 90 to 92 are vague and indefinite because the metes and bounds of the limitations "homologous" and "nGPR-x" are undeterminable.

The art of molecular biology recognizes two different proteins as "homologous" to one another if they serve analogous functions in two different organisms or appear to be of a common evolutionary origin. Because SEQ ID NO:67 appears to correspond to the amino acid sequence of a protein belonging to the G protein-coupled receptor family, one of ordinary skill could reasonably interpret this limitation as encompassing all G protein-coupled receptors, since all members in this family share certain defining structural features and analogous biological functions and are believed to be of a common evolutionary origin. However, one of ordinary skill would not believe that Applicant intends to claim any isolated member of the G protein-coupled receptor family. Therefore, an artisan of ordinary skill would be unable to distinguish between that subject matter encompassed by this limitation and that subject matter excluded by it.

Further, because the instant specification does not identify that property or combination of properties which is unique to and, therefore, definitive of "nGPR-x" an artisan can not determine if a compound which meets all of the other limitations of a claim would then be included or excluded from the claimed subject matter by the presence of this limitation.

10.2) Claim 92 is also vague and indefinite because it is unclear if the limitation "identity to a sequence of SEQ ID NO:67" requires identity to the entire sequence or just a portion of that sequence.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11) Claims 30 and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by the Kunz et al. publication (J. BIOL. CHEM. 267(13):9101-9106, 05 May 1992, cited by Applicant. The isolated protein described in Figure 3 on page 9103 of the Kunz et al. publication contains a plurality of "portion"s from SEQ ID NO:67 of the instant application and is clearly "homologous" thereto because it is also a G protein-coupled receptor, as shown by Figure 7 therein.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John D. Ulm whose telephone number is (703) 308-4008. The examiner can normally be reached on Monday through Friday from 9:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached at (703) 308-6564.

Official papers filed by fax should be directed to (703) 308-4242 or (703) 872-9306. Official responses under 37 C.F.R. § 1.116 should be directed to (703) 872-9307.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.